

Application For Research Grant

no
Date: September 29, 1955

1. Name of Investigator:

Clinton H. Thienes, M.D., Ph.D.

2. Title:

Director

3. Institution

& Address:

Institute of Medical Research, Huntington Memorial Hospital,
734 Fairmount Avenue, Pasadena 2, California

4. Project or Subject:

Effect of Daily Nicotine Administration Upon Adrenal Glands,
and Upon Mortality of the Newborn.

5. Detailed Plan of Procedure (Use reverse side if additional space is needed):

This is a two fold problem, for which much of the "raw data" have been obtained. Twenty-five pairs of rats were given twice daily injections of saline containing nicotine for a period of a year. Their litter mates (another 25 pair) were injected with saline alone, as controls. The number of young born were tabulated and a report of the effect of nicotine on fertility was made in the Journal of Pharmacology and Experimental Therapeutics, 87:1, July, 1946. A rough estimate indicated that there was a marked increase in mortality of babies born to nicotine treated mothers but the raw data on this point have never been adequately studied and evaluated.

Furthermore, data on the adrenal glands needs further evaluation. A rough estimate indicates no actual increase in size, but an increased ratio between size and adrenal weight and body surface. Earlier work, published in the Journal of Pharmacology, 46: 113, 1932, showed a ~~dx~~ decrease in body weight due to ~~dx~~ decrease in fat (hence of body surface) of nicotine injected rats, without a decrease in skeletal size. The results of our last experiments indicate therefore that the increase in adrenal weight/body surface ratio in nicotine injected rats does not indicate an actual increase in size of the adrenals, but only a decrease in the body fat. We need to recalculate our raw data to determine if this impression is true.

The second part of the problem deals with tolerance development to the effects of nicotine on the secretion or formation of the adrenomedullary hormone. Earlier, unpublished work, now realized to have been too inaccurate, indicated (1) that a

1003537080

nicotine injection decreases the epinephrine content of the adrenal gland and (2) that this effect is greatly reduced in animals chronically treated with nicotine. We would like to repeat this experiment, on rats, using modern methods of epinephrine (and nor-epinephrine) assay, both biological and chemical. The rats would be injected twice daily for six months with a nicotine-in-saline. They would then be ~~maxima~~ anesthetized with pentobarbital. The adrenals of one half of the test group and of the control group would be assayed for epinephrine and nor-epinephrine; the other half of each group would be injected with 0.5 mg. of nicotine per Kilogram body weight, and the adrenals removed 10 minutes later and assayed for the medullary hormones.

In view of the demonstrated tolerance of the central nervous system to nicotine (Jour. Pharmacol. and Exper. Therap. 48:317, 1933) it is important to know what other types of tolerance occur.

1003537081

6. Budget Plan:

Salaries + 5% Employee benefits	\$4200
Expendable Supplies	375
Permanent Equipment	250
Overhead (40% of Salaries)	1600
Other Travel & Publications	500
Total	\$6925

7. Anticipated Duration of Work:

one year

8. Facilities and Staff Available:

Animal quarters, laboratory space, kymographs, photo-electric colorimeters, Coleman Jr. Spectrophotometer, Beckman DU Spectrophotometer, constant temperature baths, etc. necessary for chemical and biological tests. Staff consists of director, head technician, secretary, animal man and varying numbers of professional and technical persons and graduate students depending on number and size of projects. A technician or two graduate students will be needed for the project on nicotine.

9. Additional Requirements:

None

10. Additional Information (Including relation of work to other projects and other sources of supply):

This project is not related to other projects of the Institute of Medical Research

s/ Clinton H. Thienes
Signature _____
Director of Project

s/ Alan R. Baldwin
Business Officer of the Institution

Recorder

Controller

1003537082